Claim 25. The method of claim 22, wherein said diagnosis or monitoring is carried out on multiple samples such that at least one analysis is carried out on a first sample and at least another analysis is carried out on a second sample.

B1 cont.

Claim 26. The method of claim 22, wherein said first and second samples are obtained at different time periods.

REMARKS/ARGUMENTS

Claims 22-26 remain in this application. Claim 22 is currently amended.

In response to the Office Action of December 3, 2002, Applicant requests re-examination and reconsideration of this application for patent pursuant to 35 U.S.C. 132.

Claim Objections and Rejections under 35 USC 112

Claim 22 stands objected to for the use of "or" as opposed to "and" in the Markush grouping. Claim 22 was further objected to for using "sulphate" as opposed to "sulfate".

The claim has been amended to obviate these objections.

Claims 22-26 further stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. On page 21, lines 11-20 of the specification, the Applicant discloses mixing a sample of a body fluid, from a mammal, with at least one compound effective to optimize the signal to noise ratio (the compound exemplified herein is heparin). On page 29, lines 13-18 of the specification, Applicant discloses that it became apparent that the addition of a polyanion was required to aid in the charge neutralization of the MBP. After optimization experiments were performed, heparin was chosen because it significantly improved the distinction between control and MS patients while maintaining an excellent signal to noise ratio with the positive control. Applicant also discloses the addition of heparin to buffer on pages 37, line 15; page 40, line 17 and pages 41 and 42. The Examiner points out that the Applicant does not disclose heparin sulphate bound to non-specific binding sites on MBP. The Examiner further indicates that there is no description in the specification disclosing heparin sulphate or heparin bound to non-specific binding sites on MBP.

Claims 22-26 further stand rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 22 at line 7, utilizes the term "effective" which is deemed to be vague and indefinite. The Examiner indicates that the term is unclear as to what is considered to be effective, and that

there is no definition or guidance in the specification for the term "effective".

Examiner Counts and his Supervisory Primary Examiner Long Le are thanked for the courtesies of an interview granted to Applicants' representative, Ferris Lander.

During the interview the objections and rejections reiterated supra were thoroughly discussed.

It was agreed to change "effective to bind" to --which binds-- in line 7 of Claim 22 in order to obviate the 35 USC 112, par. 2 rejection.

Furthermore, it was agreed to modify lines 8-11 of Claim 22 to read:

--characterized by utilizing heparin to reduce non-specific charge interactions with MBP, thereby increasing assay sensitivity-- so as to obviate the 35 USC 112, first paragraph rejection.

Applicants direct the Examiner's attention to the specification at page 42, lines 5-7:

> "Clinical detection, via sensitivity, dramatically improved when the antibody dilution buffer was modified to include heparin"

See also page 25, lines 4-10:

> "Due to the highly cationic nature of MBP, its charge may be the contributing factor for high background in a common enzyme-linked immunosorbent assay (ELISA). Non-specific charge interactions typically plague the sensitivities of ELISAs using

positively charged proteins (Pesce et al., 1986). This obstacle was recognized early during the development of the disclosed ELISA protocol."

page 41, line 21 - page 42, line 2:

"As previously mentioned MBP is a cationic protein and therefore non-specific charge interactions were hypothesized to contribute to the lack of distinction between normal and MS patient MBP autoantibody titers. Heparin (5 USP) was placed in the plasma dilution buffer due to the success with the polyclonal control (rabbit)."

and page 29, lines 13-18:

"It became apparent that the addition of a polyanion was required to aid in the charge neutralization of the MBP. After optimization experiments were performed, heparin was chosen because it significantly improved the distinction between control and MS patients while maintaining an excellent signal to noise ratio with the positive control."

Thus it is clear from the originally filed specification that the use of heparin *to reduce non-specific charge interactions with MBP, thereby increasing assay sensitivity*, as is instantly claimed, was Applicants' original intent, and such

invention was in Applicants' possession at the time of filing. Furthermore, the claims indefiniteness previously pointed out under 35 USC 112, paragraph 2, has been obviated by the amendments to claim 22 and is substantiated by the above-made reference to portions of the specification.

SUMMARY

In light of the foregoing remarks and amendment to the claims, it is respectfully submitted that the Examiner will now find the claims of the application allowable. Favorable reconsideration of the application is courteously requested.

Respectfully submitted,

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